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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Four goals were accomplished. 1) Reaction times (RTs) of monkeys and human subjects were determined for ballistic wrist flexion and extension movement made in response to visual and vibratory stimuli. 2) RTs were determined for human subjects who made wrist movements to a target after these two types of sensory stimuli were presented. 3) The relationships between the sensory responsiveness of monkey primary somatosensory cortical (SI) neurons and the magnitude of the premovement activity of these neurons were analyzed. 4) The premovement activity of non-stimulus related SI neurons was recorded to determine if the magnitude of this activity under two behavioral conditions was the same. The RT experiments indicated that humans and monkeys make movements more quickly (50-100 msec) in response to vibratory as compared to visual signals. The neurophysiological experiments suggest that sensory input to SI neurons is "gated" during behavior in regions of SI but not in others. Quantitative estimates of this gating under different behavioral circumstances are provided. Equations are described which predict the magnitude of the premovement activity during vibratory triggered trials from the vibratory responsiveness of the neurons and the amount of premovement activity exhibit in visually cued trials.

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Research Objectives:

Four research goals were accomplished during the first year of this grant. 1) We determined the reaction times (RTs) of monkeys and human subjects when they made ballistic wrist flexion and extension movement in response to visual and vibratory stimuli and correlated these findings with subject age and practice at the task. 2) We collected preliminary results on RTs for human subjects who made wrist movements to a target following these two types of sensory stimuli. 3) We analyzed the relationships between the sensory responsiveness of monkey primary somatosensory cortical (SI) neurons and the magnitude of the premovement activity of these neurons. 4) We compared the premovement activity of SI neurons that did not respond to vibratory stimuli to determine if the magnitude of this activity was related to the type of stimulus presented and the type of afferent input from the periphery that could cause these neurons to respond. The RT experiments with humans and monkeys indicate the capacities for motor performance in response to sensory cues. The neurophysiological experiments suggest that sensory input to SI neurons is "gated" during behavior and provides quantitative estimates of this gating under different circumstances.

Status of Current Research - Statement of Work:

Each of the four studies conducted involved the use of a common behavioral paradigm. This will be described in detail below. In the description of the individual studies and their findings, which will follow, any variations in this paradigm will be described.

*Behavioral Paradigm - Human Subjects:*

Young adult volunteers (ages 19-36) performed the paradigm described below. Each was asked to perform the task with their preferred hand. All had normal or corrected-to-normal vision and had normal hearing. These subjects received no compensation for their participation in this study.

Subjects were seated in a specially designed chair in a quiet, moderately lit (5 foot-candles) room and viewed a visual display placed 50 cm directly in front of them at eye level. This display contained 31 light-emitting diodes (LED) located behind a smoky-grey acrylic plate. The display consisted of a central, larger, red light-emitting diode and vertical rows of smaller, yellow LEDs. The display was coupled to the output of a wrist position transducer. Each successively illuminated LED above or below the central lamp corresponded to an angular deflection of 1° from the central position. The subject's hand rested on a flat aluminum handle coupled at one end to the axle of a brushless DC torque motor while the forearm was supported by an arm rest.

Each trial was initiated by the subject centering the handle so that the central LED was illuminated. The handle had a 0.12 Nm load assisting extension. At the start of each trial a combination of two instruction LEDs were lit. These were located in the upper left corner of the visual display (8.3° of visual angle from the center). The presence or absence of illumination of each instructed the subject about the direction of the required movement (a red LED; on-extension; off-flexion) and the type of sensory stimulus that would be presented in that trial (a green LED; on-visual; off-vibratory). These also forewarned the subject that a trial had started. The subject had to maintain a centered wrist position for a randomly chosen time period (0.5-2.0 s). If the subject maintained a steady position within ±0.5° (each lamp =1°) of center, a vibratory or visual stimulus was presented and the current wrist position was designated as the start

position for analysis. Vibratory cues consisted of vibrating the handle by driving the motor with a low-amplitude sine wave (less than 100μ peak-to-peak measured 10 cm coupling of the handle to the motor) at either 27, 57 or 127 Hz. Visual cues consisted of adding or subtracting a DC voltage from the coupled wrist position signal, resulting in a shift in the illuminated lamp (±1.7° of visual angle from display center) in the opposite direction from the requested movement by an amount equal to that required to re-center the display (5.0°). Either sensory stimulus remained on until the subject moved at least 5° from the start position. Subjects received an audible "click" if the movement was made in the appropriate direction. This click informed the subject that the trial was successful and also served as a signal for the subject to re-center the handle to begin the next trial. On the first training day each subject was instructed to make the wrist flexion and extension movements as quickly as possible. The speed and amplitudes of these ballistic movements were not restricted other than by stops in the apparatus at ±30° of angular deflection from center.

Flexion and extension movements were requested in alternating blocks of ten trials each. Vibratory and visual stimuli were randomly presented within blocks for a given vibratory stimulus frequency. Three groups of at least 120 trials were collected daily. In each group, the vibratory stimulus frequency was held constant and the visually-cued trials randomly distributed. The total duration of these manipulations was about 20-30 minutes.

*Behavioral Paradigm - Primate Subjects:*

Four adult male rhesus monkeys (*Macaca mulatta*) , 8-10.9 kg, were also used in the present experiments. They were cared for in accordance with the *NIH Guide for Care and Use of Laboratory Animals, revised 1985*. Each monkey was seated in an acrylic primate chair and trained to make the same wrist flexion or extension movements described above. These movements were made against or with a 0.07 Nm load assisting extension. They viewed the same visual display used for the human subjects. The display was placed 35 cm directly in front of them at eye level. At this distance the instruction and visual cue LEDs were 11.8° and ±2.4° of visual angle from the display center, respectively. The monkeys received a fruit-juice reward (along with the "click") for each correctly performed trial. In all other respects, the monkeys performed the same tasks as the human subjects.

Monkeys were first trained to perform wrist flexion and extension movements in response to vibratory cues only. Once each animal reached a stable level of performance (determined by the lack of statistically significant differences in the mean RTs for successive days), visually-cued trials were randomly interposed with vibratory-cued trials. After an initial period during which the animals learned to make the appropriate movements in response to either type of cueing stimulus, their performance again stabilized.

*Neurophysiological recording:*

Once the animals had reach a level of steady behavioral performance, they were prepared for SI single-unit electrophysiological recording. A stainless steel chronic recording chamber and head restraint device were surgically implanted (Nelson, 1988; Nelson and Douglas, 1989). Transdural penetrations were made daily into the cortex using platinum-iridium microelectrodes. The neuronal activity was amplituded, filtered and discriminated by conventional means. The analog signal corresponding to the animal's current wrist position was sampled at 100Hz. This information data related to the timing of behavioral events and neuronal activity, were collected and stored in a microcomputer. Graphic and numerical displays of the neuronal activity and wrist position were

reconstructed by an off-line data analysis routine. These were used to select the neurons included in two the studies described below.

1) Reaction Times For Ballistic Movements:

Forty trials for each of the three vibratory go-cue frequencies (total 120) and a similar number of visually cued trials were analyzed for each subject on a daily basis. Only those trials with RTs between 100 and 600 msec were considered. The daily mean RTs for vibratory and visually-cued trials along with daily standard deviations and standard errors were calculated for data from each of the two stimulus-cue conditions. No statistically significant differences were observed in the daily RTs across trials triggered by the three vibratory-cue frequencies. Therefore, the RTs from all daily vibratory-cued trials were combined and the mean RT for these trials was compared to those triggered by the visual cues for each direction of subsequent movement.

*A. Human Reaction Times-*

Figure 1A shows the combined performance of eleven human subjects for flexion wrist movements made in response to visual (LS - Lamp Shift) and vibratory (Vib) go-cues. From the first training day subjects made movements in response to vibratory cues more quickly than in response to visual cues. From training day 4 on, the differences in mean RTs for similar movements were significantly different (ANOVA, $\rho<0.05$) and the significance of the difference improved with further practice.

To determine when the subjects, as a population, reached stable performance on each type of stimulus-movement trial pairing, the mean RTs for day N were subtracted from those for day N-1 and a paired t-test was performed on the resulting values. The differences in RTs for the same stimulus-movement trial pairing for the total subject pool ceased to be significantly different (prob.=0.05) on training day 5 for vibratory-cued flexion, on day 6 for vibratory-cued extension and visually-cued flexion and on day 7 for visually-cued extension. These measures indicated the day on which the subjects' performance became relatively stable. Individual subjects showed further behavioral improvement up until day 9. Since each subject had reached stable performance by training day 9, the mean RTs for each condition for training days 9-14 were averaged to yield each individual's final mean RTs under the four stimulus-movement conditions. Movements of either wrist flexion or extension made in response to vibratory cues were consistently associated with shorter RTs than those made in response to the visual cues. The mean differences for the population of eleven subjects were 47.80 msec for flexion movements and 45.53 msec for extension movements. All differences in RTs for each individual subject and for the population were significantly different (prob.=0.001; independent t-test; table 1).

The differences in RTs were plotted against the age of each subject. This was done to test the possibility that the differences in RTs during vibratory as compared to visually cued trials might be related to the age of the subject. Figure 1B illustrates the relationship between the mean differences in RTs during flexion trials as a function of subject age. The difference in RTs increased as a function of subject age and the relationships for flexion and extension RT differences could each be described by a simple linear relationship with correlation coefficients of $r=0.48$ and $r=0.59$ for flexion and extension trials differences, respectively. The correlation between the differences in RTs and subject age for extension movements was statistically significant (Spearman correlation coefficient 0.658; $\rho<0.05$) whereas the measures were not significantly correlated for flexion movements (Spearman correlation coefficient 0.438; $\rho=0.13$).

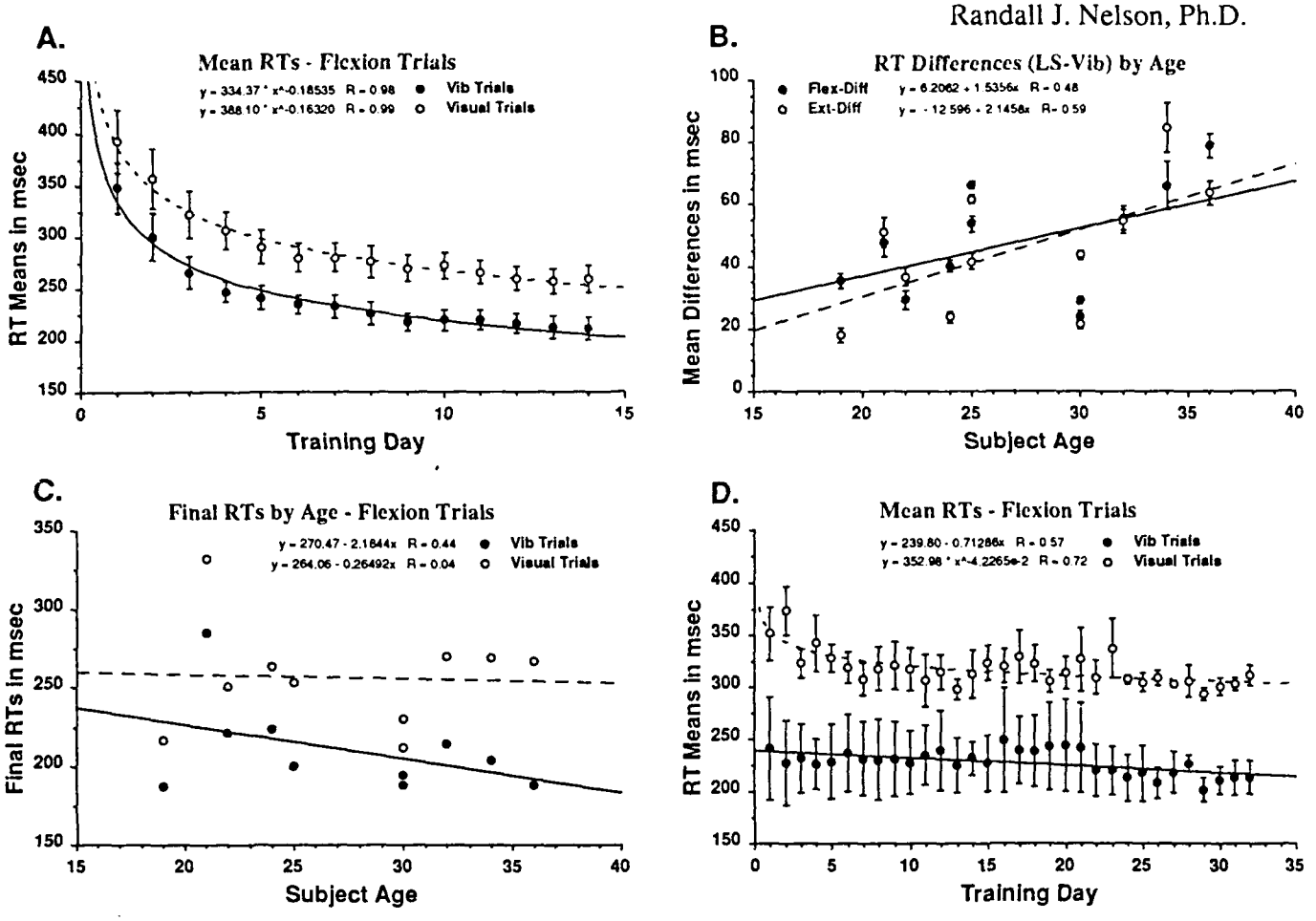


*Figure 1. A. The daily mean RTs for 11 human subjects as a function of training day for flexion trials. B. The differences in final mean RTs for 11 human subjects as a function of subject age. C. The final mean RTs for visual and vibratory cued flexion trials for 11 human subjects plotted as a function of subject age. D. The daily mean RTs for 4 monkeys as a function of training day for flexion trials. Shown are the best fit log and linear functions and their coefficients for these data. A., C. & D., Solid lines indicate the fit of these data for vibratory cued trials; dashed lines indicate the fit for visually cued trials. B. Solid line = Flexion trial differences; dashed line = extension trial differences. Bars indicate standard errors of the means. A. With increased training the RTs improved and there was a decrease in the variability as shown by the decrease in the standard errors. B. RT differences for similar movements made in response to visual as compared to vibratory cues increased as a function of subject age. C. While the RTs for visually cued trials did not consistently vary across the ages tested, final mean RTs for vibratory trials decreased as a function of subject age. D. With increased training the RTs improved and there was a decrease in the variability as shown by the decrease in the standard errors.*

The final mean RTs were then plotted against subject age. We sought to determine if the differences in RTs were related to either increases or decreases in visual or vibratory RTs, respectively. Figure 1C illustrates these data for flexion trials along with the linear relationships of the RTs as a function of age. While the RTs for visually cued trials did not consistently vary with age, there was a slight improvement in the RTs for vibratory cued trials in older subjects. Thus, the overall increase in the RT differences as a function of age may be related to a decrease in the RTs for vibratory cued trials.

TABLE 1

A. Final Ballistic Mean RTs for:

| | VIB Flex | VBF sem | VIB Ext | VBE sem | LS Flex | LSF sem | LS Ext | LSE sem |
|---|---|---|---|---|---|---|---|---|
| *11 Humans* | 215.88 | 9.81 | 214.06 | 9.74 | 263.69* | 11.99 | 260.93* | 12.78 |
| *4 Monkeys* | 213.30 | 5.11 | 215.98 | 6.95 | 303.40 | 3.09 | 325.36 | 5.67 |

B. Differences in Ballistic Mean RTs for:

| | Flex Difference | Flex sem | Ext Difference | Ext sem |
|---|---|---|---|---|
| *11 Humans* | 47.80* | 5.37 | 45.53* | 6.12 |
| *4 Monkeys* | 90.09 | 10.08 | 109.38 | 11.73 |

C. Final Targeted Mean RTs for:

| | VIB Flex | VBF sem | VIB Ext | VBE sem | LS Flex | LSF sem | LS Ext | LSE sem |
|---|---|---|---|---|---|---|---|---|
| *5 Humans* | 219.10 | 11.58 | 215.30 | 9.36 | 277.36* | 11.14 | 272.96* | 7.49 |

D. Differences in Targeted Mean RTs for:

| | Flex Difference | Flex sem | Ext Difference | Ext sem |
|---|---|---|---|---|
| *5 Humans* | 57.51* | 1.89 | 57.73* | 1.89 |

*Table 1. **A. & B.**: Final mean RTs and differences between the two stimulus-response conditions (Visual-Vibratory) for ballistic movements made by humans and monkeys. **C. & D.**: Final mean RTs and differences between the two stimulus-response conditions for targeted movements made by humans. SEM = standard error of the mean. * = difference between the RTs for ballistic vs. targeted movements significant (prob.<.003; independent t-test). All RTs for movements in the same direction for the two stimulus groups were significantly different (prob.<.001; independent t-test).*

*B. Monkey Reaction Times-*

Figure 1D illustrates the pooled mean daily RTs for the four monkeys, plotted as a function of training day. Monkeys made reaction time movements more quickly in response to vibratory as compared with visual cues. The progress of their performance could be described by the best-fit log and linear functions listed in this figure. From the twenty-second training day on, the difference in mean RTs for flexion and extension movements were consistently significantly different (ANOVA, $\rho<0.05$). There was a slight improvement in each animal's behavior from this day on. Differences in mean RTs reach a significance level of $\rho<0.02$ level on 8 of the remaining 10 days. Paired t-tests of the daily mean RTs for day N minus the mean RTs for day N-1 ceased to be significantly different (prob.=0.05) on the twenty-second training day as well. In general, after reaching stable performance, each animal had longer RTs for visually cued trials as compared to vibratory cued trials. As was found for the human subjects, monkeys made reaction time flexion movements of the wrist 90.09 msec sooner in response to vibratory as compared to visual cues. For extension movements, RTs were shorter by an average of 109.34 msec for vibratory as compared to visual cues. All differences in RTs for each individual subject and for the population were significantly different (prob.=0.001; independent t-test; table 1).

It was not possible to correlate the animals RTs differences with their ages since accurate ages were not available for all animals. However, the ages of the first three monkeys were known to be between 5-8 years whereas the fourth monkey was 14 years old. The difference between the final RTs for extension

movements made to visual as compared to vibratory signals was noticeably longer for this older monkey than for the three younger ones.

*Conclusions-*

Human subjects initiated movements approximately 50 msec sooner in response to vibratory as compared to visual cues. For monkeys, this difference was approximately 100 msec. Mean daily RTs for monkeys and human subjects improved with practice until they reached a steady level of performance. Increased differences between RTs for vibratory and visually cued movements were weakly correlated with increased age of the human subjects. This appeared to be due to better performance (decreased RTs) by older subjects on vibratory cued trials while RTs for visually cued movements did not consistently vary across the age range of subjects tested (19-36 yrs). The results obtained using this novel paradigm suggest that it may be a useful tool for simultaneously testing behavioral performance or neurological function during somatosensorimotor and visuomotor tasks. A report of the work conducted in this study has been submitted for publication and has been returned for revision (see listing of written publications).

2) Reaction Times For Targeted Movements:

Five human subjects performed a wrist flexion and extension paradigm similar to that described in section 1. The major difference between this and the previous paradigm was that the subjects had to move to align the cursor of the display with a target corresponding to a position 5 degrees from the centered position. In visually cued trials, this target was illuminated after the hold period and remained on until the subject properly aligned the handle. In the vibratory cued trials, the handle was vibrated at the same time that the visual target came on. During both types of trials the subject was required to maintain the new position for 0.5 sec before he or she received a "click" indicating that the trial had been successful. This was done to determine if increasing the complexity of the task (requiring accurate movements by the subject) increased the RTs in comparison with ballistic movement trials. In addition, we could assess the effects of practice upon behavioral performance.

*Human Reaction Times-*

Figure 2 illustrates the pooled mean daily RTs for five human subjects. As with the first study, the subjects' behavior improved with increased practice. To determine when the subjects reached stable performance on each type of stimulus-movement trial pairing, the mean RTs for day N were subtracted from those for day N-1 and a paired t-test was performed on the resulting values. The differences in RTs for the same stimulus-movement trial pairing for the total subject pool ceased to be significantly different (prob.>0.10) on training day 10 for vibratory-cued flexion and vibratory-cued extension. For visually-cued flexion and visually-cued extension, mean RTs were not statistically different after day 4. These measures indicated the day on which the subjects' performance became relatively stable. Each subject's final mean RTs were calculated by averaging the mean RTs for each stimulus-response condition for days 10-14. In general, as in the ballistic movement study, subjects initiated movements more quickly in response to vibratory as compared to visual cues alone. The mean RT differences were 57.51 and 57.73 msec for flexion and extension movements, respectively (table 1D). The final RTs for targeted movements made in response to vibratory cues were not significantly different from those for ballistic movements made to the same stimuli (table 1C). The RTs for targeted movements made to visual cues alone were

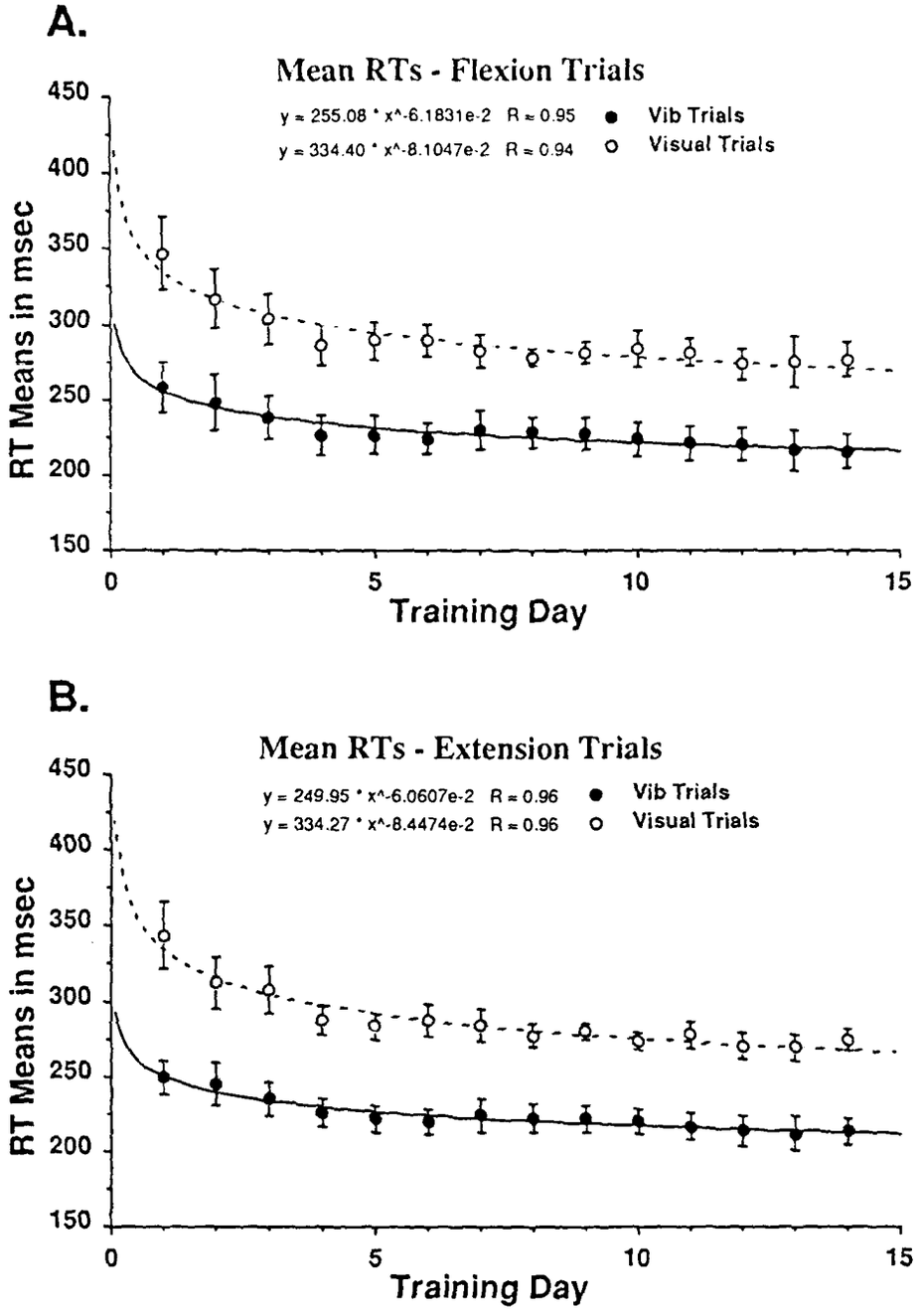


*Figure 2. The daily mean RTs for 5 human subjects who performed wrist flexion and extension movements from a center zone to a target 5° from the centered position. A. Flexion RTs; B. extension RTs. Open circles; RTs for trials begun in response to visual cues. Closed circles; RTs for trials in response to vibratory go cues. Bars indicate standard errors of the mean. Best fit log functions for these data are listed along with their correlation co- efficients. The amount of variance explained by the function can be calculated by taking the square root of the R value. These subjects made flexion and extension movements more quickly in response to vibratory as compared to visual cues. Daily mean RTs, calculated as the average of the RTs for all subjects on that training day, were not significantly different after the 4th day for visually cued trials. For vibratory cued trials they were not different after the 10th training day.*

longer than for ballistic movements by 10-12 msec. This difference was statistically significant (prob.<.003; independent t-test).

*Conclusions-*

Subjects initiate movements more quickly in response to vibratory as compared to visual cues. This is true even when, regardless of the cue, they must move to the position indicated by a visual target. It is

possible that with movements of larger amplitude, more complex movement requirements or increased sensory distraction, the difference in RTs may be even greater. Studies addressing these issues are currently being planned. In addition, monkeys are being trained to perform targeted movements tasks to determine if they exhibit the same response time differential and if they will continue to be a good model for studying the neurophysiological substrates that underlie these differences in performance and their relationship to the changes in sensory responsiveness that occur during the initiation and execution of wrist movements. A report of this work will be submitted for publication once a larger population of subjects has been studied.

3) Relationships Between Sensory Responsiveness and Premovement Activity:

We sought to determine if the sensory responsiveness of SI neurons was correlated with the magnitude of the premovement activity that these neurons exhibit during behavior. To do this, data analysis was conducted in several stages. Perievent histograms, raster displays of the neuronal activity and analog displays of the animal's behavioral performance were examined, with these displays oriented in time either with the onset of the sensory stimulus or with the onset of the sensory-triggered movements. To determine the level of background activity under each condition, the discharge on each neuron was measured during the period in which the animal held a constant position. This was considered to be the background activity of the neurons during each phase of the task. Neuronal activity associated with the onset of vibratory stimuli was measured by determining the first change in activity after stimulus onset in which the magnitude of the change was at least ±50% of the background activity for at least 20-30 consecutive milliseconds. Premovement activity was measured from displays centered on movement onset using the same temporal and magnitude criteria. All measures of neuronal activity were expressed as the mean discharge rate during their respective periods in spikes per second. Stimulus related and premovement activity changes were then normalized by subtracting the background activity from each, yielding the change in activity from background that occurred in association with these phases of the task.

The neurons included in this study all met certain selection criteria. Each exhibited a short latency (often less than 30 msec) response associated with vibratory stimulus onset. Each then showed a decrease in activity from the level associated with stimulus onset, often returning to near background levels. Each also had a clearly discernible change in activity that occurred prior to movement onset. Finally, each neuron had a peripheral receptive field that was located on the hand or the wrist of the forelimb that was used to make the behavioral response. Neurons with cutaneous and deep receptive fields were analyzed separately. A total of 166 area 1 and 61 area 3b neurons which had stimulus related changes in activity were examined. Of these 55 area 1 and 18 area 3b neurons met all the criteria stated above. Since most of these neurons were tested using more than one vibratory stimulus frequency and since these neurons often exhibited different magnitudes of cue and premovement related activity depending upon the frequency of the vibratory go-cue, the records of each neuron for each stimulus frequency were considered separately. This resulted in the inclusion of 133 and 57 area 1 and area 3b "sub-units", respectively, that met the selection criteria.

Figure 3 illustrates the task related activity of two SI neurons. Panels A. & C. are for an area 3b neuron that responded to passive extension of the second digit at the metacarpophalangeal joint. Panels B. & D. are for an area 1 neuron with a cutaneous receptive field located on the third palmar pad. The upper panels show the activity of these neurons centered on the onset of the vibratory cue.

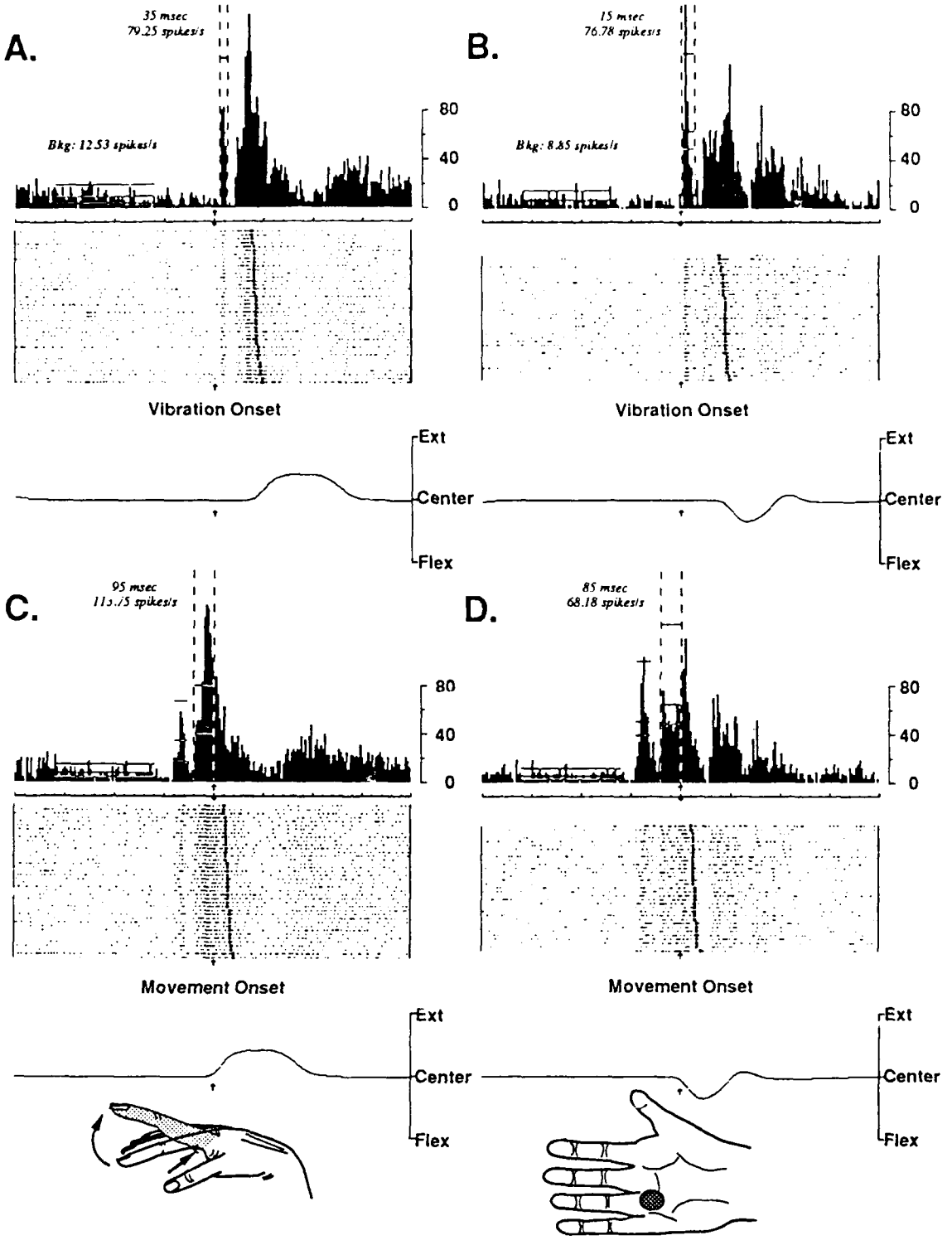


*Figure 3. Task related activity of two SI neurons. Panels A. & C.: An area 3b that responded to passive extension of the second digit at the metacarpophalangeal joint. Panels B. & D.: An area 1 neuron with a cutaneous receptive field located on the third palmar pad. Upper panels show the activity of these neurons centered on the onset of the vibratory cue. Background activity and the stimulus related changes in discharge rate are listed. Both neurons had a short latency phasic response to the onset of vibration. Bottom panels show the same trials centered on movement onset. Each neuron had non-stimulus related changes in activity prior to movement onset.*

The background activity and the stimulus related changes in discharge rate are listed. Both neurons had a short latency phasic response to the onset of vibration. The bottom panels show the same trials centered on movement onset. Each neuron had a non-stimulus related change in activity that occurred prior to the onset of movement.

One way to determine if the vibratory responsiveness of SI neurons is correlated with the magnitude of their premovement associated discharge is to statistically compare the magnitudes of these two activity changes. The first assumption made was that increased responsiveness to peripheral stimuli presented as cues for movement is associated with increased discharge rates associated with stimulus onset. The data were grouped by the cortical area in which the recorded neurons were located, the direction of movement (wrist flexion or extension) that was subsequently made in response to the vibratory cue stimuli and the type of RFs that each neuron had (either cutaneous or deep). The magnitude of the stimulus response was plotted against the magnitude of the premovement acitivty change for each neuron within these groups. Non-parametric correlation analyses were performed on the population of area 3b and 1 neurons examined in this study. Spearman Rank Correlation analyses were conducted on these sample populations because there was no a priori reason to assume that the relationships would be linear. In general, the magnitude of the premovement activity was positively correlated with the magnitude of the vibratory response for area 1 neurons having either cutaneous or deep receptive fields during flexion movements. This movement was against the load and in the direction of the stimulated surface of the hand. For extension movements, which were away from the stimulated hand surface and assisted by the load, only the area 1 neurons with cutaneous receptive fields showed a positive correlation between vibratory responsiveness and premovement activity magnitude. The premovement activity of area 1 neurons during extension movements that received input from deep receptors appeared to be negatively correlated with vibratory responsiveness. The correlation coefficients for each group of area 1 neurons were statistically significant ($\rho<=0.05$) with three of the four groups showing a high degree of correlation ($\rho<0.001$). The vibratory responsiveness of area 3b neurons was not correlated with the premovement activity during any of these movements.

Our initial assumption was that the premovement activity of SI neurons may be related to their capacity to respond to peripheral stimuli. The hypothesis that we favored was that if cortical neurons respond to vibratory stimuli and if those stimuli are constantly present until after a wrist movement has begun, the information that these neurons signal to other parts of the CNS may actually interfere with the monitoring of the movements themselves. Therefore, we assumed that the CNS may "gate-out" this information, suppressing it just before the movement. We also assumed that when monkeys make wrist movements in response to visual stimuli, no interference would occur so that the CNS would not suppress the activity of vibratory responsive neurons.

To determine the relationship between sensory responsiveness and premovement activity in SI neurons, we examined our data using factor analysis and multiple regression statistics to see if we could construct a model equation that would predict the magnitude of the premovement activity from other parameters that we measured. Factor analysis indicated that between 65-99% of the variance in the premovement activity could be accounted for by just two factors. The weightings of these analyses suggested the following equation as a good predictor of the magnitude of premovement activity:

*(1) PM activity= constant +* $\alpha$ **vibratory responsiveness +* $\beta$ **visual trial premovement activity*

This relationship assumes that the visual trial premovement activity reflects the movement related activity that occurs when vibration is not present and that the vibratory responsiveness is reflected by the initial activity associated with the onset of the vibratory stimulus. Using multiple regression analysis, we found the relationships between vibratory responsiveness and premovement activity listed in table 2.

Table 2

| Condition | Constant | α | β | R^2 |
|---|---|---|---|---|
| *Area 1* | | | | |
| Flex-Cutaneous (N=36) | -14.767** | 0.412* | 0.895◊ | 0.653 |
| Flex-Deep (N=10) | -33.620** | 0.727◊ | 0.635◊ | 0.755 |
| Ext-Cutaneous (N=29) | -23.038** | 0.297* | 1.063◊ | 0.782 |
| Ext-Dee, (N=23) | -8.090** | 0.313‡ | 0.890◊ | 0.839 |
| *Area 3b* | | | | |
| Flex-Cutaneous (N=6) | 87.964** | -1.189** | 0.611◊ | 0.818 |
| Flex-Deep (N=10) | -2.139** | -0.003** | 1.121◊ | 0.951 |
| Ext-Cutaneous (N=7) | -39.995** | 0.470** | 1.470◊ | 0.847 |
| Ext-Deep (N=6) | 2.280** | 0.025** | 0.943◊ | 0.997 |

*Table 2. The results of multiple regression analysis using equation 1. Listed are the relationships derived from only those neurons for which a full set of vibratory and visually cued trials were recorded. Symbols: *‡= not different from 0.0; *= different from 0.0 and 1.0; ◊= different from 0.0 but not from 1.0; ‡= not different from 0.0 yet different from 1.0. Probability level for significance; 0.001. Conditions list the direction of movement and the type of receptive fields which these neurons have. R^2 is a measure of the variance accounted for by the regression equation.*

Examples of the "goodness of fit" of these equations can be seen in figure 4. Simplifying table 2 by replacing the listed values with 0, 1 or the actual value, based upon the statistical significance of the magnitude of the constants and coefficients we derived the values in table 3.

Table 3

| Condition | Constant | α | β |
|---|---|---|---|
| *Area 1* | | | |
| Flex-Cutaneous | 0.0 | 0.412 | 1.0 |
| Flex-Deep | 0.0 | 1.0 | 1.0 |
| Ext-Cutaneous | 0.0 | 0.297 | 1.0 |
| Ext-Deep | 0.0 | 0.0 | 1.0 |
| *Area 3b* | | | |
| Flex-Cutaneous | 0.0 | 0.0 | 1.0 |
| Flex-Deep | 0.0 | 0.0 | 1.0 |
| Ext-Cutaneous | 0.0 | 0.0 | 1.0 |
| Ext-Deep | 0.0 | 0.0 | 1.0 |

*Table 3. The results of multiple regression analysis using equation 1 and replacing the values by 0, 1 or the actual value based on their statistically significant effects upon the described relationships.*

These results suggest several interesting relationships between the sensory responsiveness of SI neurons and the magnitude of the premovement activity that they exhibit. First, the magnitude of the

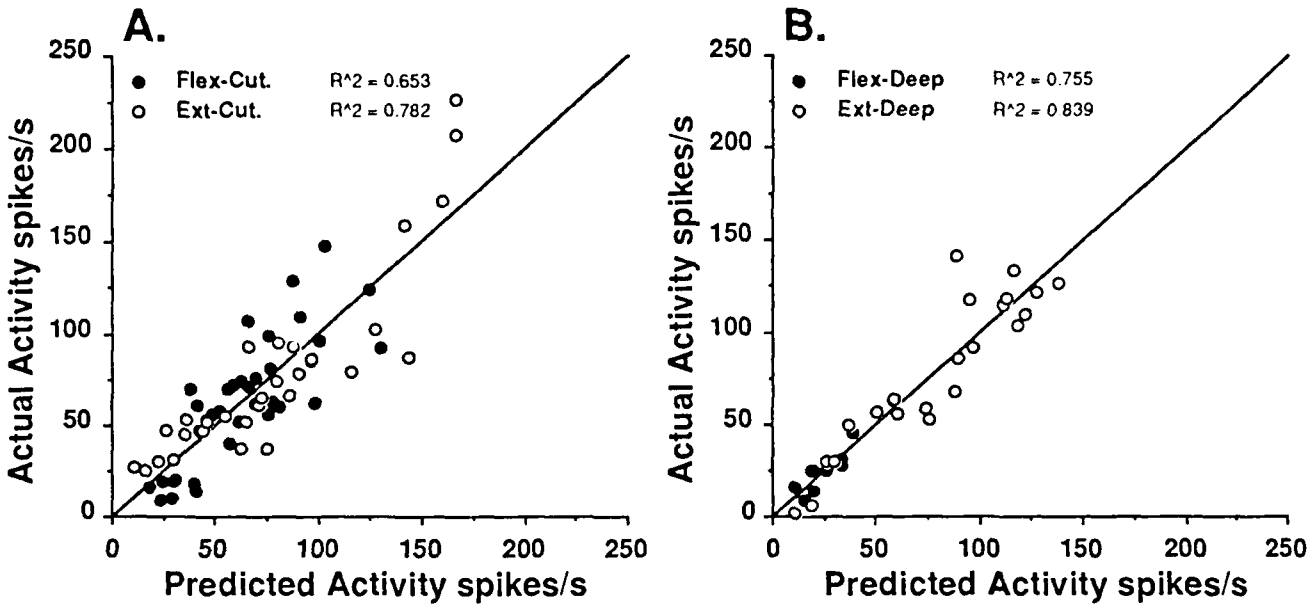


*Figure 4. Plots of the premovement activity magnitudes predicted by the use of equation 1 against the measured premovement activity magnitudes for all area 1 neurons studied. A. The comparison for neurons having cutaneous RFs. B. The results for neurons having deep RFs. A. & B. Open circles indicate values for extension trials; closed circles indicate values for flexion trials. R^2 values indicate the amount of variance that can be accounted for by the linear functions described in table 2. Between 65-84% of the variance in the premovement activity of area 1 neurons can be described using equation 1 with the constants and coefficients listed in that table.*

premovement activity of area 3b neurons during vibratory cued trials is not different from that exhibited during visually cued trials. This is in keeping with the fact that one factor in the equation, the vibratory activity, was not correlated with premovement activity. Second, for area 1 neurons with cutaneous RFs, the premovement activity is equal to the movement related activity plus some fraction of the vibratory activity. Since the vibratory signals remain present until after the movements are made, it is possible that following an initial activity burst at stimulus onset, the neurons are suppressed (figure 3). Then, just before the movement, the suppression is lifted, but not completely, as indicated by the less than unity coefficients of the equations. Third, area 1 neurons having deep RFs show an interesting relationship that may be related to movement direction and force or the surface of the forelimb that is stimulated. When the movement is toward the stimulated hand surface and/or opposing a load, the coefficient of the vibratory component of the equation is best described by 1.0. When the movement is away from the stimulus and/or assisted by the load, the coefficient is 0.0.

*Conclusions-*

The premovement activity of SI neurons can be predicted using equation 1, provided that the vibratory responsiveness and the neurons' capacity for premovement activity in the absence of vibration are known. We are currently evaluating models of circuitry that could account for our observations. The one that we favor involves gated vibratory input. In this model for area 1 neurons,

the gate would be intially open at stimulus onset, closed approximately 60 msec after the neuron responds to the vibration and then re-opened just before the beginning of the movement. The movement related input would arrive at the neurons prior to movement and not be modulated by the modality of the stimulus. This gate must be modulated to account for the partial reactivation of the vibratory response observed for neurons with cutaneous RFs. It is possible that either the gate is not re-opened for area 3b neurons or that the area 3b neurons studied had intrinsic properties that caused them to rapidly adapt to the stimulus and then be refractory to further activity for a period longer than it takes to begin the movement. This and other models are being evaluated. A final determination of the best model for these observations awaits further data collection as we especially need more area 3b neurons of this type before accurate assessments can be made. A report of this work is currently in preparation.

4) Relationships Between Premovement Activity Under Two Conditions:

In our experiments we have collected a large number of recordings from neurons that did not respond to either vibratory or visual stimuli. Many of these not only exhibited premovement activity but also had either cutaneous or deep RFs. We examined the possibility that the premovement activity of these neurons might be different depending upon the modality of sensory stimuli used to elicit the wrist movements. The paradigm used was identical to that described in section 3. and these recordings were collected from two of the monkeys involved in that study. Measurements of premovement activity and background activity during vibratory and visually cued trials were made as previously described. Records were grouped by the frequency of the vibratory stimulus, the movement made and the type of RFs that the neurons had. This "sub-unit" grouping resulted in the inclusion of 121 area 1 and 53 area 3b recordings. The premovement activity for visually cued trials was plotted against the corresponding trials where vibration was the movement cue. If the premovement activity of these populations was the same, then scattergrams of these activities should be linearly related and the resulting best-fit equations should have a slope of 1.0. To determine the slope of the linear best-fit function for these data, the following equation was used:

*(2) Vibratory premovement activity = constant + $\alpha$* visual trial premovement activity*

The results of these analyses are listed in table 4. Examples of scatterplots are seen in figure 5.

In general, the premovement activity in area 3b neurons was the same regardless of the modality of the stimulus used to elicit the movements. Two exceptions are noted. For neurons with cutaneous RFs, a significant difference in the relationship between the premovement activity in visual and vibratory cued trials was observed (coefficient = 0.713). The size of this population was small and the data are, therefore, suspect. In addition, only one neuron having deep a RF was recorded at 127Hz vibratory stimulus frequency. While the exact nature of the relationship between premovement activity for area 3b neurons awaits the collection of additional data, our tentative conclusion is that there is no difference in premovement activity during vibratory and visually cued trials.

Area 1 neurons with cutaneous RFs had no significant difference in premovement activity during visual and vibratory cued trials. In comparison, there was a significant difference in the activity for neurons having deep RFs. The probabilities that the listed coefficients were different from 1.0 in

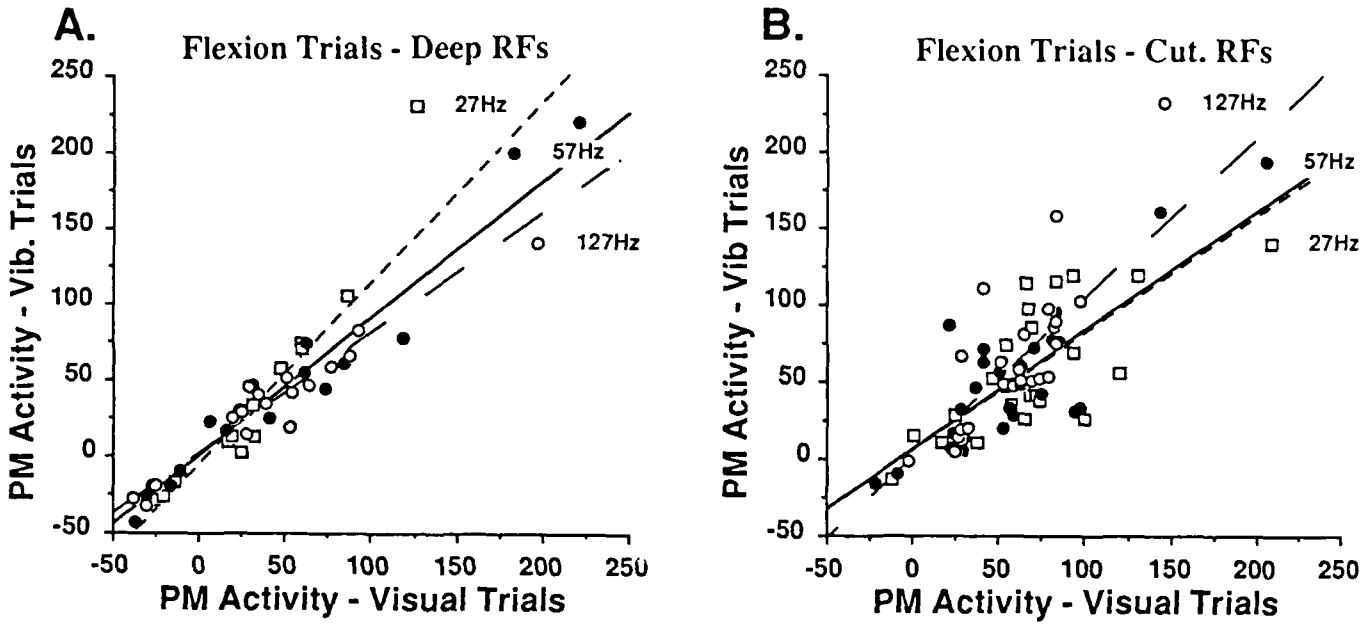


*Figure 5. The premovement activity of area 1 neurons during visually cued trials plotted against that recorded during vibratory cued trials. A. The magnitudes recorded for neurons with deep RFs before flexion movements. B. Premovement activities for neurons receiving cutaneous input. Short dashed lines and open squares: 27Hz vibration; solid lines and solid circles: 57Hz; long dashed lines and open circles: 127Hz. Values for the relationships between visual and vibratory trial premovement activity are given in table 4. Only the slope of the linear regression for 127Hz flexion trials for deep receptive neurons was significantly different from 1.0. A less than unity slope of these functions is interpreted to indicate that the premovement activity is suppression in vibratory as compared to visually cued trials.*

flexion trials were 0.06, 0.09 and 0.01 for 27, 57 and 127Hz stimulation trials, respectively. For extension trials, these probabilities were 0.004, 0.331 and 0.0001. The smallest values for the coefficients were for vibratory cues of 127Hz, regardless of movement direction.

*Conclusions-*

It has previously been shown that vibratory stimuli of higher frequencies (100Hz and above) have the ability to entrain the firing of neurons receiving input from muscle spindles which signal information about the length of a muscle. These receptors are thought to be important in providing information about the execution of limb movements by the nature of their response to active muscle contraction. It is possible that the presence of vibration at frequencies capable of activating these receptors may result in erroneous information about the state of muscles involved in a subsequent movement. We speculate, based on our results, that at higher vibratory stimulation frequencies, the activity of neurons with deep RFs may be suppressed prior to movement. This would explain why the premovement activity in vibratory cued trials using a 127Hz vibratory signal is less than that during visually cued trials. It, however, does not explain the nearly significant differences seen for the coefficients for the other frequencies used during flexion trials, nor the significant difference in premovement activity observed for extension movements using a 27Hz stimulus. A more general hypothesis is that all area 1 neurons receiving input from deep receptors have their premovement

**Table 4.**

| CONDITION | N= | Const | $\alpha$ | R^2 |
|---|---|---|---|---|
| *Area 1 Cutaneous RFs* | | | | |
| Flex-27Hz | 24 | 6.121** | 0.763‡ | 0.453 |
| Flex-57Hz | 28 | 6.532** | 0.776‡ | 0.516 |
| Flex-127Hz | 23 | 1.117** | 1.040‡ | 0.499 |
| Ext-27Hz | 18 | 2.231** | 0.794‡ | 0.825 |
| Ext-57Hz | 29 | 1.492** | 0.945‡ | 0.900 |
| Ext-127Hz | 21 | 3.779** | 0.815‡ | 0.762 |
| *Area 1 Deep RFs* | | | | |
| Flex-27Hz | 13 | -4.907** | 1.181‡ | 0.941 |
| Flex-57Hz | 17 | 0.375** | 0.896‡ | 0.942 |
| Flex-127Hz | 16 | 2.108** | 0.786* | 0.894 |
| Ext-27Hz | 11 | 0.320** | 0.885* | 0.990 |
| Ext-57Hz | 21 | -6.693** | 0.950‡ | 0.950 |
| Ext-127Hz | 18 | 5.468** | 0.773* | 0.959 |
| *Area 3b Cutaneous RFs* | | | | |
| Flex-27Hz | 11 | 6.005** | 0.713* | 0.900 |
| Flex-57Hz | 15 | 0.607** | 1.044‡ | 0.982 |
| Flex-127Hz | 14 | 5.462** | 0.822‡ | 0.818 |
| Ext-27Hz | 12 | 4.706** | 1.000‡ | 0.957 |
| Ext-57Hz | 13 | 0.904** | 1.098‡ | 0.936 |
| Ext-127Hz | 14 | -1.755** | 0.976‡ | 0.884 |
| *Area 1 Deep RFs* | | | | |
| Flex-27Hz | 4 | -5.609** | 1.258‡ | 0.996 |
| Flex-57Hz | 5 | 1.000** | 1.122‡ | 0.990 |
| Flex-127Hz | 4 | -0.589** | 0.670‡ | 0.912 |
| Ext-27Hz | 7 | 2.157** | 0.856‡ | 0.990 |
| Ext-57Hz | 4 | 37.497* | 0.167‡ | 0.054 |
| Ext-127Hz | 1 | NA | NA | NA |

*Table 4.. The results of regression analysis using equation 2.. Listed are the relationships derived from only those neurons for which a full set of vibratory and visually cued trials were recorded. Symbols: **= not different from 0.0; *= different from 0.0 and 1.0; ‡= not different from 1.0. Probability level for significance; 0.001. Conditions list the direction of movement, the stimulus frequency and the type of receptive fields which these neurons have. R^2 is a measure of the variance account for by the regression equation.*

activity modulated when vibration is present whereas area 1 neurons receiving cutaneous input are not modulated. These conclusions are tentative and will be strengthened by larger sample populations. A preliminary report of these finding has been published (see listing of written publications).

General Statement:

The demonstration of the differences in RTs for identical wrist movements made in response to visual as compared to vibratory cues may also prove to be of great benefit if the task requirements include not only the fastest response to external events but also the necessity to abort a movement based on changing environmental conditions. It is clear that movements made in response to vibratory cues have the advantage of being executed more quickly. There may be other factors which make the presentation of information by vibratory cues desirable. In many tasks which involve the control of devices by hand movements, the subjects are already preoccupied with the visual and auditory environment. Additional visual cues may distract from visual fixation on devices that are of crucial

importance for the task at hand. Auditory warning signals may interfere with ongoing communication required during the normal execution of motor events. Vibratory signals have a slight disadvantage in that the information content of these signals is low compared with the spectrum of different qualities and quantities of visually and auditory information. For some applications, however, vibratory information processing may have the distinct advantages of being non-interfering and resulting in faster processing times. It remains to be determined what are the appropriate stimulus parameters for vibratory stimulation during complex tasks. If presented at too high an amplitude or at the wrong frequency, vibratory signals may degrade motor performance by entraining the receptors which provide information about the current position of the limb and the muscle tension in that limb . This does not appear to be the case for low amplitude vibratory signals presented to the palm of the hand. In this study, because no differences were seen in the actual movements made to either vibratory or visual cues. Therefore, if properly presented, the use of vibratory signals may provide important additions to the repertoire of the modes of information processing. These signals may be useful especially in the control of complex devices that require a constant state of vigilance on the part of the subject controlling these devices.

The relationships between vibratory related and premovement activity may give important insight into the underlying mechanisms of sensorimotor integration. This is also true of the relationships between premovement activity under differing sensory stimulus conditions. The mechanisms controlling movements made in response to sensory cues have been suggested to consist of at least three stages. First the triggering input must be perceived and perhaps stored briefly, second the appropriate response must be related to the signal, and finally, the response must be executed. Each stage of the stimulus-triggered movement response is probably under the influence of central modification which may alter a neuron's activity during any or all of these stages. Central modification may be related to conditions in the external and internal behavioral environment which directly affect the initiation, execution and outcome of the desired behavior. For example, the degree to which an animal or subject is selectively attentive to sensory stimuli through expectation or distraction may determine whether a sensory cue is perceived. Different motor commands for the attainment of the same behavioral goal may be generated depending upon the current state of the animal's limb that will eventually make the motor response. The execution of the motor command may also be relayed to sensory centers to inform them that the subsequent sensory feedback is the result of a self-generated movement as opposed to perhaps an experimentally produced perturbation of the limb. Welford suggests that mechanisms controlling movement operated "...as if there is a 'gate' between the first and the second stages which prevents data passing to the second stage while it is 'busy'" (Welford, 1974). It is further postulated that such a gate is opened upon receipt of signals that indicate that the appropriate behavioral response has begun.

While this theoretical approach to the understanding of sensory-triggered motor response provides a framework which shapes our thinking, many of its components are difficult to test experimentally. If such a gate exists, then there should be neurons with activity patterns that might be predicted by this model. This would suggest that there are neurons which respond to sensory stimuli, then exhibit a change in activity perhaps related to the closing of the gate and finally show another activity change, presumably related to the gate opening during the early phases of the execution of a movement. We have observed activity patterns for neurons in the primary somatosensory cortices of monkeys which are reminiscent of the activity that might be predicted by this model. The location and nature of this

"gate", however, are still unknown. We, and other investigators, have some evidence to suggest that the gating of sensory inputs occurs mainly at the cortical level. Through further experimentation, we hope to uncover additional relationships of the integration of sensory events and motor commands and we eventually hope to determine where sensory gating signal arise.

Welford, A. T. (1974) Behavioral approach to motor programming: On the sequencing of action. Brain Res. *71:* 381-392.

Status of Future Research:

We are currently training monkeys to perform the ballistic movement task prior to training them on the targeted movement task. We have approached their training in this manner because human subjects report that the latter task is more difficult to perform. We will continue to assess the monkeys' behavior on the first task, and collect RT data in the process. Next, we will start training them on the latter task. If the performance of any individual animal is not acceptable, he will be used to collect additional data on area 3b neurons recorded during the ballistic task. As soon as we have an animal capable of performing the targeted movement task, we will begin neurophysiological recording from SI neurons.

We plan to expand our human psychophysical experiments on targeted movement to include movements of larger and randomly varied amplitudes. In addition, we will train subjects to alter their movement strategies based upon whether they perceive a second (kinesthetic) stimulus occurring just before movement (See third series of experiments proposed in original grant application). In this way we will determine the effectiveness of changes in sensory responsiveness in filtering out sensory information prior to the onset of active movement and whether this filtering can be "overriden" if the information is important to the outcome of the desired behavior.

Listing of Written Publications-

R. J. Nelson. Set related and pre-movement related activity in primate primary somatosensory cortical neurons depends upon stimulus modality and subsequent movement. Brain Res. Bull. 21(3):411-424, 1988.

R. J. Nelson and V D. Douglas. Changes in premovement activity in primary somatosensory cortex differ when monkeys make hand movements in response to visual vs. vibratory cues. Brain Res. 484:43-56, 1989.

R. J. Nelson, C. A. McCandlish and V. D. Douglas. Reaction times differ for hand movements made in response to visual vs. vibratory cues. Somatosensory and Motor Research (submitted and returned for revision).

Presentations of Supported Work-

R. J. Nelson and V. D. Douglas. Quantitative differences in premovement activity of primary somatosensory cortical neurons during visual versus vibratory cued hand movements. Neuroscience Abst. 14:716, 1988.

Workshop Organizer "Sensory responsiveness varies as a function of the behavioral state under which stimuli are presented". Winter Conference on Brain Research - 1989.

Submitted Abstracts-

R. J. Nelson and V. D. Douglas. Differences in sensorimotor integration in cortical areas 3b and 1 of the monkey. Neuroscience Abst. (submitted).

V. D. Douglas and R. J. Nelson. Reaction times differ when humans and monkeys make hand movements in response to visual as compared to vibratory cues. Neuroscience Abst. (submitted).

Associated Personnel-

Vickie Douglas has been employed as a Research Assistant during the first year of this grant. She participates in all functions of the laboratory and has been of crucial importance in analyzing the data presented in this report. She understands all aspects of the research and the concepts derived from the results.

Interactions-

Meetings attended:
1988 Meeting of the Society for Neuroscience, Toronto, Ontario, Canada - November, 1988.
1989 Winter Conference on Brain Research, Snowbird, Utah - Jan.-Feb., 1989

New Discoveries-

None.